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Experiences of renal transplants from donors with renal cell carcinoma after *ex vivo* partial nephrectomy

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Purpose: Routine evaluation of kidney donors occasionally reveals an incidental renal mass with an otherwise satisfactory kidney function. The use of such a kidney with an enhancing mass for transplantation is a matter of debate owing to a possible risk of transmission of donor malignancies. We report our experience of kidney transplants from donors with renal cell carcinoma, after *ex vivo* resection of the renal mass.
Methods: Two women aged 44 and 56 years were diagnosed with enhancing renal masses measuring 0.9 cm and 0.7 cm, respectively, during donor evaluation for kidney transplantation. Both patients and their families were informed of a potential risk of recurrent renal cell carcinoma following transplantation.
Results: Renal function test results of both donors satisfied the living donor selection criteria. Laparoscopic live donor nephrectomy was performed with *ex vivo* resection of renal masses on the bench table. Immediate pathological analysis revealed a renal cell carcinoma with a margin of normal renal parenchyma before transplantation. Regimens based on mammalian target of rapamycin inhibitors, which are known for their antitumoral properties, were used for immunosuppression in both recipients. None of the recipients showed recurrence or metastasis during the follow-up period, which was longer than 3 years after transplantation.
Conclusion: In light of the ongoing shortage of kidney donors, kidneys with small renal cell carcinoma could be considered for transplantation after appropriate removal of the lesion, with a very low risk of recurrent disease.
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Key Words: Kidney transplantation, Renal cell carcinoma, Nephrectomy

INTRODUCTION

Kidney transplantation is the treatment of choice for patients with end-stage renal disease (ESRD), as it offers better long-term survival compared with that offered by other dialysis treatments [1]. However, there is a considerable deficit of organ donors owing to disparity between the demand and supply of kidney transplantation. Thus, various donor sources have been explored to increase the number of patients who could benefit from renal transplantation. The criteria for "acceptable" deceased donors have been extended to include older donors and donation after cardiac death donors [2]. Despite these efforts, there has been a slight improvement in the availability of transplantable kidneys, and several patients die every year while waiting for kidney transplantation [1]. Not only shortage of deceased donors but also better long-term function of living donor allografts has encouraged patients with ESRD to consider potential living donors [1,3].

The routine evaluation of potential kidney donors occasionally reveals incidental renal masses arising from the donor kidney. The transplantation of a living donor kidney with an enhancing renal mass is controversial and is considered a high-risk procedure. We report 2 cases of renal transplantation from donors with an enhancing renal mass, in which laparoscopic

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nephrectomy was performed followed by *ex vivo* partial nephrectomy.

METHODS

Two women aged 44 and 56 years were diagnosed with enhancing renal masses measuring 0.9 cm and 0.7 cm, respectively, during donor evaluation for kidney transplantation (Fig. 1). Both donors were informed of the available therapeutic options, including partial nephrectomy, and total nephrectomy with kidney donation. Benefits of partial nephrectomy over radical nephrectomy without any disadvantage in survival rates were also informed to both donors [4].

The patients and their families opted for kidney donation. The procedures were approved by the Ethical Committee of Korea University Anam Hospital and adhered to the 1975 Declaration of Helsinki. Both patients provided written informed consent. The renal function test results of the donors satisfied the living donor selection criteria (creatinine levels, 0.67 mg/dL and 0.59 mg/dL; estimated glomerular filtration rate, 100 mL/min and 112 mL/min). The left and right kidneys of the patients were removed laparoscopically, and ex vivo resection of the renal cell carcinoma was performed prior to transplantation, under a surgical microscope. Intraoperative examination of the frozen section revealed a renal cell carcinoma with negative surgical margin. The tumor type was clear cell carcinoma in one woman and papillary renal carcinoma in the other woman. Both were low-grade tumors and their pathologic stage was pT1a.

Surgical technique

The kidneys were removed via hand-assisted laparoscopic surgery. Following nephrectomy, back-table kidney perfusion was initiated using HTK solution (Custodiol, Dr. Franz Koehler Chemie GmbH, Alsbach-Haehnlein, Germany). During back-table preparation, the range of the resection margin was marked using intraoperative ultrasonography; the renal mass was then excised and sent for routine histological examination. The defect was then closed using a running 4-0 Vicryl suture. The donor kidney was transplanted to the right iliac fossa of the recipient using the running suture technique to the external iliac artery and vein. The ureter was anastomosed to the bladder using the Lich-Gregoir technique.

RESULTS

Two recipients aged 52 and 34 years with ESRD undergoing hemodialysis due to hypertensive nephrosclerosis and chronic glomerulonephritis respectively, received these kidneys after ex vivo resection of small RCC. Potential of recurrence and associated risk of donor-transmitted cancer ($0\% < f \leq 0.1\%$) [5] were fully informed before transplantation. Cancer specific survival rates at 5 and 10 years (97.8% and 95.8%, respectively) of renal cell carcinoma treated with partial resection were informed to donors and recipients as well [4].

The partially nephrectomized kidneys were successfully transplanted in the recipients, and both renal perfusion and function were excellent after transplantation. The cold ischemic time in the patients aged 52 and 34 years was 82 and 63 minutes, respectively. To minimize the risk of tumor recurrence in our recipients, Rapamune was administered while mycophenolate was withdrawn at 1 month after renal transplantation.

The final creatinine levels of the recipients were 0.87 and 0.98 mg/dL, and the postoperative creatinine levels of the donors were 1.10 and 0.90 mg/dL. Abdominal computed tomography performed 1 year after transplantation showed neither signs of local recurrence of renal cell carcinoma nor metastasis. None of the donors showed any evidence of tumor recurrence, and the recipients have shown no signs of graft rejection so far.

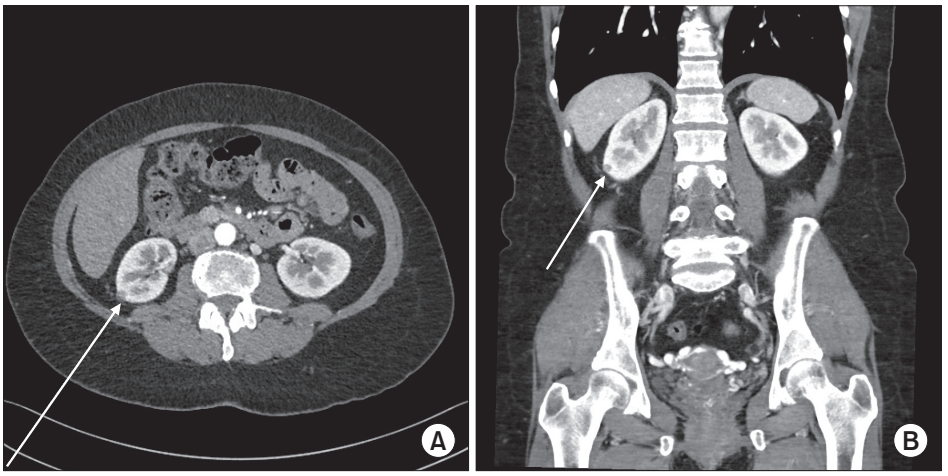

Fig. 1. (A) Transverse abdominal computed tomography angiogram of the 44-year-old kidney donor shows 0.9 cm tumor in the mid pole of the right kidney (arrow). (B) Coronal abdominal computed tomography angiogram of the 56-year-old kidney donor shows 0.7 cm tumor in the lower pole of the right kidney (arrow).

DISCUSSION

There has been a dramatic increase in the incidence of small and localized renal tumors over the past few decades. Most renal tumors detected using ultrasound or CT are incidental findings when abdominal imaging is performed for unrelated symptoms [6]. For several years, the standard management for suspected renal carcinoma was radical nephrectomy in the context of a normal contralateral kidney. However, longitudinal studies showed that the risk of local recurrence and metastatic spread in pT1 renal tumors was extremely low [7]. Moreover, on the basis of the favorable oncological outcomes reported with partial nephrectomy in patients with a solitary kidney or in those with a compromised contralateral kidney, partial nephrectomy has become a popular treatment method for sparing renal mass [7-9]. Thus, partial nephrectomy is recommended for tumors less than 4 cm. In addition, partial nephrectomy is increasingly being used in transplant recipients with *de novo* renal cell carcinoma within the kidney graft. Despite the requirement for immunosuppressive therapy, partial nephrectomy was performed in selected transplant patients [10-13]. Thus, a donor kidney with a small tumor can be transplanted after ex vivo resection.

Although these kidneys are clearly outside the standard criteria for donor organs and would otherwise have been discarded in the past, kidney transplantation after resection of the tumor has recently been reported as a treatment option with acceptable results. Nicol et al. [14] reported 43 recipients who received kidneys with small, localized, incidentally discovered renal mass (5 deceased and 38 live donors) after back-table partial nephrectomy. With a mean follow-up period of 32 months, only one of the allografts showed possible tumor recurrence, which occurred 9 years after transplantation. These authors recently demonstrated improved survival of these patients who underwent transplantation in comparison with the group of patients on the transplantation waiting list [15]. Similarly, Mannami et al. [16] reported that 8 kidneys with small renal mass were transplanted after ex vivo resection and the recipients were followed up for up to 135 months, with no recurrence or metastasis observed during that period.

These promising results encouraged us to perform tumor resection and transplantation instead of nephrectomy in donor patients. The decision was made based on the small and localized (pT1) renal cell carcinoma and the fact that no metastasis was detectable at the time of donor evaluation.

The use of immunosuppressive agents after transplantation could lead to a higher incidence of cancer in transplant recipients compared with that in the general population [17]. Current standard regimen for long-term immunosuppression comprises a calcineurin inhibitor combined with mycophenolate and prednisolone. Recently, mammalian target of rapamycin (mTOR) inhibitors such as everolimus and sirolimus have been used as alternative agents for mycophenolates [18]. These mTOR inhibitors have been shown to be effective for the treatment of metastatic renal cell carcinoma, and compared with other immunosuppressive therapies, they reduce the prevalence of renal cell carcinoma in the graft kidney following transplantation [14,19,20]. Therefore, long-term use of an mTOR inhibitor should be considered for immunosuppression in recipients who are at risk for renal cell carcinoma.

The results of the present study suggest that kidneys with small incidental tumors can be transplanted in selected patients, after careful pathological examination and appropriate surgical excision. These patients might benefit from using an mTOR inhibitor-based regimen for immunosuppression because of its antitumoral effects in renal cell carcinoma. Despite the advantages of using kidneys after removal of the tumor, the potential risk of recurrent disease is a concern when kidneys with renal cell carcinoma are used for transplantation. Hence, the recipients should maintain routine follow-up for imaging studies to ensure that there is no tumor recurrence or to exclude metastasis.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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